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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,644	10/29/2003	David S. Garvey	102258.133 US2	4077
25270	7590	10/26/2005	EXAMINER	
EDWARD D GRIEFF HALE & DORR LLP 1455 PENNSYLVANIA AVE, NW WASHINGTON, DC 20004			AULAKH, CHARANJIT	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 10/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/695,644

Applicant(s)

GARVEY, DAVID S.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33, 35-48, 50-59, 61-70, 72-82, 84-87 and 89-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-33, 35-48, 50-59, 61-70, 72-82, 84-87 and 89-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. According to paper filed on Sep. 16, 2005, the applicants have canceled claims 34, 49, 60, 71, 83, 88 and 93-108 and furthermore, have amended claims 1-4, 6, 7, 24, 25, 33, 35, 36, 39, 40, 48, 50, 51, 59, 61, 62, 70, 74, 80, 84, 87 and 91.
2. Claims 1-33, 35-48, 50-59, 61-70, 72-82, 84-87 and 89-92 are now pending in the application.

Response to Arguments

3. Applicant's arguments filed on Sep. 16, 2005 have been fully considered but they are not persuasive regarding enablement rejection, most of indefiniteness rejections and obviousness rejections. The applicants have not amended claims 1 and 2 to delete non-elected subject matter. In regard to enablement rejection, the examiner did not question enablement but scope of enablement. The specification is enabling for treating hypertension using instant compounds of formulae I, IV and V. However, the examiner does not agree with the applicants arguments that the specification is enabling for treating every known vascular disease using instant compounds of formulae I, IV and V alone or in combination with other compounds. The instant compounds are beta-adrenergic receptor antagonists. There is no teaching either in the specification or prior art references provided to show well known utility of beta-adrenergic receptor antagonists either alone or in combination with other drugs in treating every known vascular disease. The instant compounds of formulae I, IV and V encompass hundreds of thousands of compounds and therefore, in absence of such teachings and guidance, it would require undue experimentation to demonstrate the efficacy of instant

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compounds alone or in combination with thousands of other drugs in known animal models of every known vasculae disease and hence their utility for treating these disease conditions.

In regard to indefiniteness rejections, the applicants have amended claims to overcome some indefiniteness rejections. However, the examiner does not agree with the applicants arguments regarding definiteness of following terms:

In claims 1 and 2, it is not clear how the NO or NO₂ group is attached to the structure of Nebivolol? The applicants have amended claims to address this issue. However, this is still not clear. Can NO or NO₂ group also attach to O atom present in the ring?

In claims 6, 24, 39, 50 and 61, the term –vascular diseases due to nitric oxide insufficiency – is indefinite.

In claims 15, 76, 90 and 92, the specific compounds which donate, transfer or release nitric oxide, or induce the production of endogenous nitric oxide etc. are not defined.

In claim 19, the specific compounds comprising ON-O, ON-N etc. are not defined.

In claims 33 and 91, the specific antioxidants are not defined.

In claim 48, the specific nitrosated compound is not defined.

In claims 59 and 91, the specific compounds for treating cardiovascular diseases are not defined.

In claims 78 and 79, the target site is not defined.

In regard to obviousness rejection, the examiner does not agree with the applicants arguments that it would not have been obvious to one skilled in the art to arrive at the instant claimed invention. As stated clearly in the last office action, Loscalzo teaches a

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method of treating vascular diseases due to nitric oxide insufficiency by administering nitrosated beta-adrenergic blockers including Nebivolol and Von Lommen teaches increased beta adrenergic receptor blocking activity of Nebivolol as compared to other known beta-adrenergic blockers. Therefore, one skilled in the art would have been motivated to select nitrosated Nebivolol as beta-adrenergic blocker due to its greater efficacy as taught by Von Lommen.

Conclusion

4. Rejections under 35 U.S.C. 112, first paragraph, 35 U.S.C. 112, second paragraph and 35 U.S.C. 103(a) are maintained for the reasons of record.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

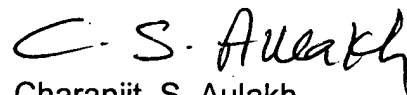
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is

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(571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charanjit S. Aulakh
Primary Examiner
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